

REMARKS

With this amendment, claims 1-5, 35, 37, and 78-93 are pending. Claims 89 and 93 are presently amended. Support for these amendments can be found in the specification, p. 17, line 6 through p.18, line 28.

I. 35 U.S.C. 102(b)

Reconsideration is requested of the rejection of claims 1, 2, 78, 79, 81, 82, 84, 85, and 89-91 under 35 U.S.C. 102(b) as being unpatentable over JP 10298089 ("JP '089") or Gourvest et al. (U.S. Patent No. 5,525,594).

Claims 1 and 85 are generally directed to methods of treating an organism for a condition mediated by COX-2 expression. The methods comprise administering to the organism having such a condition a composition comprising a COX-2 inhibiting amount of an extract of *Vitex agnus castus*.¹

JP '089 discloses a cell adhesion inhibitor containing effective amounts of ingredients of plants from the families Apocynaceae, Moraceae, and/or Smilacaceae, or extracts thereof. It is disclosed that this inhibitor may be used as an anti-allergic agent, immunosuppressor, or cancer metastasis inhibitor.

JP '089 does not disclose an organic extract of *Vitex agnus castus* or the administration of the same to an organism suffering from conditions mediated by COX-2 expression. Thus JP '089 fails to disclose each and every element of claims 1 and 85, and accordingly, does not anticipate claims 1 and 85.

Gourvest et al. disclose purification of the compound oenotheine B from extracts of *Epilobium parviflorum*, *Oenothera*

¹ Claim 1 is directed toward selective inhibition of COX-2 via administration of an organic extract of an edible plant. Due to the election of species requirement, however, only extracts from the genus *Vitex* and of the species *agnus-castus* are presently under consideration.

erythrosepala, *Eucalyptus alba*, all three being of the family Myrtales, and *Woodfordia fruticosa*, of the family Lythraceae. Oenotheine B is disclosed as having the activity of inhibiting 5 α -reductase, which is an enzyme responsible for the conversion of testosterone into dihydrotestosterone, and as having a beneficial effect in the treatment of benign hyperplasia of the prostate, cancer of the prostate, and certain androgen-dependent illnesses, including disorders linked to hyperandrogenism, acne, androgenic alopecia, seborrhea, and female hirsutism.

Gourvest et al. do not disclose an organic extract of *Vitex agnus castus* or the administration the same to an organism suffering from conditions mediated by COX-2 expression. Thus Gourvest et al. fail to disclose each and every element of claims 1 and 85, and accordingly, do not anticipate claims 1 and 85.

Claims 2 and 78, 79, 81, 82, and 84, which depend from claim 1, and claims 89-91, which depend from claim 85, are patentable over JP '089 and Gourvest et al. for the reasons stated above with respect to claims 1 and 85 and by reason of the additional requirements which they introduce.

II. 35 U.S.C. 103(a)

Reconsideration is requested of the rejection of claims 1-5, 35, 37, and 78-93 under 35 U.S.C. 103(a) as being unpatentable over JP 2000236835 ("JP '835") taken with EP 248215 ("EP '215") and JP 56020597 ("JP '597").

As stated in greater detail above in Section I, claims 1, 3, and 85, are directed to methods of treating an organism for a condition mediated by COX-2 expression.

The full abstract of JP '835, enclosed herewith, discloses a composition comprising Koto-sugi as the "main raw material" and five other secondary components, one of which is *Vitex agnus castus* rhizomes. The *Vitex agnus castus* containing component of the composition may exist as a powder or as a "liquid

concentrate," the liquid concentrate being obtained by boiling the *Vitex agnus castus* containing component of the composition in water (i.e., an **aqueous** extraction). It is disclosed that the composition is "believed to be good for health, especially for the prevention of cancer."² JP '835 does not disclose the administration of an **organic** extract of *Vitex agnus castus* to an organism suffering from a condition mediated by the expression of COX-2, the administration of the compound in a COX-2 inhibiting amount, or the use of the same to selectively inhibit COX-2. (1) 102

EP '215 discloses the use of an ethanol extract of *Vitex agnus castus* to treat hyperprolactinemia, a condition which, to applicants' knowledge and the art of record, is not mediated by COX-2 expression. The reference does not disclose the administration of an organic extract of *Vitex agnus castus* to an organism suffering from a condition mediated by the expression of COX-2, the administration of the compound in a COX-2 inhibiting amount, or the use of the same to selectively inhibit COX-2. 7

The full abstract of JP '597, enclosed herewith, discloses the compound EK, obtained from an n-hexane extract of a plant belonging to the genus *Eucalyptus*. JP '597 also states that the compound has "an anti-inflammatory action." This reference does not disclose the administration of an organic extract of *Vitex agnus castus* to an organism suffering from a condition mediated by the expression of COX-2, the administration of the same in a COX-2 inhibiting amount, or the use of an organic extract to selectively inhibit COX-2.

The Office has failed to establish a *prima facie* case of obviousness, as the references, when combined, fail to teach each and every element of the claims.³ Specifically, as discussed

² JP 2000236835 Abstract.

³ MPEP §2142.

above, each of these three references fails to teach the administration of an organic extract of *Vitex agnus castus* to a person suffering from a condition mediated by COX-2, the administration of the same in a COX-2 inhibiting amount, or the use of the same to selectively inhibit COX-2. As each individual reference fails to teach each of these elements, it cannot be asserted that the combination of the three cures this deficiency. Therefore, because the combination of references fails to teach or suggest all such claim limitations, the Office has failed to establish a *prima facie* case of obviousness.⁴

In addition, the Office has failed to establish a *prima facie* case of obviousness as there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to modify or combine the reference teachings.⁵ Specifically, JP '835 would suggest to one of skill in the art that it is the Koto-sugi that possess the desired anti-cancer activity since it is disclosed to be the "main raw material" of the extract. Therefore, such a disclosure would lead one of skill in the art away from the claimed invention directed not to the use of Koto-sugi, but to the use of an organic extract of *Vitex agnus castus* to treat an organism suffering from a condition mediated by COX-2 expression.

Moreover, JP '089 suggests using a composition obtained by the **aqueous** extraction of *Vitex agnus castus*. As there is no certainty that the activity asserted to be obtained by the aqueous extraction of *Vitex agnus castus* would also be obtained by an organic extraction of the same, JP '089 would not motivate one of skill to extract *Vitex agnus castus* with an organic

⁴ MPEP §2142.

⁵ MPEP §2142.

solvent instead of water. Instead, JP '089 would lead one of skill in the art away from the presently claimed invention.

Likewise, EP '215 fails to recognize that an organic extract of *Vitex agnus castus* may be used to treat COX-2 mediated conditions in an organism suffering from the same. The only disclosure therein of the administration of an extract of *Vitex agnus castus* is the administration of the same to a patient suffering from hyperprolactinemia for the treatment of the same. A reference that discloses the use of the extract for the treatment of a condition in **no way disclosed** to be associated with COX-2 expression would not motivate or suggest to one of skill in the art to combine the same reference with JP '835 that discloses (1) an **aqueous** extract of a composition wherein (2) the "main raw material" is something **different** from that of EP '215.

JP '597 does not provide the motivation or suggestion that is lacking from JP '835 and EP '215. The disclosure of the use of n-hexane as an organic solvent for extraction of *Eucalyptus* does not motivate one of skill in the art to combine this disclosure with the other two above-mentioned references, as it does nothing to suggest that the use of an organic solvent to extract *Vitex agnus castus* would achieve an extract that could be used according to the claims of the present application. If anything, one of skill in the art would have been led away from the presently claimed invention, as one would be lead to believe from the three cited references that a combination of the disclosure in JP '835 of n-hexane as a solvent with the disclosure in JP '597 of an aqueous extract of *Vitex agnus castus* would achieve nothing more than the disclosure contained in EP '215 - namely, an organic extract of *Vitex agnus castus* that is useful for the treatment of hyperprolactinemia.

Accordingly, none of three cited references provides the requisite motivation or suggestion to combine it with either or both of the other two cited references. Any attempt to attain

the presently claimed invention through the combination of the above-mentioned references is only possible through impermissible hindsight and the use of applicants' specification as a guide to piece together the various aspects of the invention. This is in clear contradiction to the law.⁶ Accordingly, because there is no motivation or suggestion within the references themselves to modify or combine the reference teachings, the Office has failed to establish a *prima facie* case of obviousness.⁷

Claims 2 and 78-84, which depend from claim 1, claims 4-5, 35, and 37, which depend from claim 3, and claims 86-93 which depend from claim 85, are patentable over JP '835 taken with EP '215 and JP '597 for the reasons stated above with respect to claims 1, 3, and 85 and by reason of the additional requirements which they introduce.

⁶ *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988).

⁷ MPEP §2142.

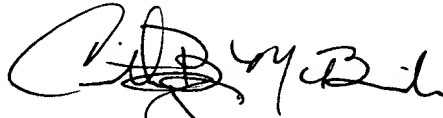
CONCLUSION

In light of the above arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 2, 78, 79, 81, 82, 84, 85, and 89-91 under 35 U.S.C. 102(b) and of claims 1-5, 35, 37, and 78-93 under 35 U.S.C. 103(a).

Applicant requests an extension of time to and including July 27, 2003, for filing a response to the above-mentioned Office action. A check in payment of the applicable extension fee is enclosed.

The Commissioner is hereby authorized to charge any deficiency or overpayment in connection with this amendment to Deposit Account No. 19-1345.

Respectfully submitted,



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